

THE UNIVERSITY OF WISCONSIN
COLLEGE OF AGRICULTURE

Madison 6

DEPARTMENT OF GENETICS

27 October 1947.

Dear Evelyn,

Thank you very much for so promptly and kindly sending your manuscript in response to my request. I notice that you have altered the title from chemicals affecting nucleic acids, to chemical agents, which is of course very wise. (However, could one not say, perhaps with tongue in cheek that even NaCl is a chemical affecting, at least, nucleoproteins?) Your hinted results with NaCl are very interesting indeed in view of the postulated indirect effect of desoxycholate, perhaps via the mineral metabolism of the cell which we discussed last summer. Keep up the very good work.

As you know, it is my personal opinion that your attention to details such as testing for possible selectional effects by treating mixed populations is the most outstanding feature of your recent work. Tell me, however, whether you or anyone has thought to verify the general technique for assaying V_1 mutants (better, V_1^r mutants) by adding a small, measured number of cells from a V_1^r culture to a large population of V_1^s cells and recovering after lysis of the V_1^s population an increase in the count of resistant colonies equivalent to the added V_1^r 's? The only reason that I can think of, a priori, that this might not work is that toxic products or whatnot may be released by lysing cells. It is not enough to assay mixtures of V_1^r and V_1^s in roughly equal proportions. The experiment is, really, necessary to round out the empirical verification of the general technique.

By your comment on the relation between toxicity and mutagenic activity do you refer to the possibility that it may be cell products released during the killing of the cell that are involved. That could be checked by determining the influence of diluting the treated suspensions. Don't you think that a mutagen would have to be lethal, on the basis that probably most genes even in a bacterium are concerned with some indispensable process, so that unless there were some determinate effect, the majority of mutations should be lethal?

You mention going on to test induced reversion of biochemical mutants of B/r. Would double (two-step) mutants of same be any particular help to you? I isolated some last summer, including Y38 (arginine), Y-39 (histidine), Y43 (arginine + methionine), Y44 (histidine + pab) Y49 (arginine + tyrosine). Give me the word and I'll have them sent to you. As I remember these all do revert at convenient rates. On the other hand I would want to try to convince you of the value of mutants of K-12, of which there is a large repertoire now, and in which of course genetic tests for recombination are easily done. I trust that Newcombe deposited strains Y40 and Y53 with you at the lab with instructions on using them. These will be published very soon anyhow in Genetics.

At Yale, Ray Barratt tried out desoxycholate on Neurospora, and found no toxicity at pH 7.5, and found toxicity but no marked mutagenic activity at lower pH's. Esther got equally negative results in preliminary attempts to induce reversion in Neurospora inositolless, although in her work with Giles effects of X-ray, uv, mustard and radiophosphorus were easily established. So let me know whether you can find an effect on biochemical mutants of coli.

My job here is primarily research. Today is the first day I've been able to do any work. I plan to continue studies on transformations in E. coli, and am setting up a program in collaboration with Biochemistry to test the genetic control of glycosidases in coli K-12, with the view, among other things of testing the ~~1:1~~ 1:1 theory. So far the only contribution is that two recurrences of a lactose-negative phenotype have been genetically identical. There are a lot of people on the campus, however, who are very much interested in the genetic aspects of their own organisms, such as Phytonomas, Venturia, Glomerella, and the smuts, and I expect that I may be dabbling with some of these too. The only teaching, aside from a routine quiz section in elementary genetics is my seminar on microbial genetics, which seems to be working out very well in conveying something of genetic ideas to the graduate students in departments such as biochem., plant path., and agric. bacter. There is certainly a phenomenal amount of interest here in genetic microbiology, but except for G. Keitt, in Plant Pathology, no one has done anything about it. My present lab quarters are rather temporary and very inadequate, but a new one is in the blueprint stage, involving some remodelling, and may be ready in 8-12 mos.

Back to your paper: I notice on the first page a reference to methylcholanthrene and Neurospora. It may be too late, but I would recommend that you check again with Tatum about that. When I left, he was expressing a considerable amount of reservation about the results.

I'll send it back as soon as I can. Thanks again. Best regards to the lab crew;

Sincerely,

Joshua.